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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/527,026	03/16/00	WEST M	000270-111

000909
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HM12/1011

EXAMINER	
WOITACH, J	
ART UNIT	**PAPER NUMBER**
1632	11

DATE MAILED: 10/11/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/527,026	Applicant(s) WEST ET AL.	
	Examiner Joseph Woitach	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-68* is/are pending in the application.

4a) Of the above claim(s) *40-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This an original application filed March 16, 2000, which claims benefit to provisional applications; 60/179,486, filed February 1, 2000, and 60/152,340, filed September 7, 1999.

Applicants preliminary amendment, filed March 16, 200, paper number 5, has been received and entered. The specification has been amended.

Election/Restriction

Applicant's election without traverse of group I, claims 1-39, in Paper No. 9 is acknowledged.

Claims 40-68 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 9.

The requirement is deemed proper and is therefore made FINAL.

Claims 1-68 are pending, claims 40-68 are withdrawn from consideration as being drawn to a nonelected invention, and claims 1-39 are currently under examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The correction of citizenship for Jose Cibelli is not signatured and dated. It was not executed in accordance with either 37 CFR 1.66 or 1.68.

Specification

The disclosure is objected to because of the following informalities: The specification contains several references to a URL (for example: page 6, line 7; page 8, line 20). The attempt to incorporate subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference (See MPEP 608.01(p)).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of providing primary cells comprising: a) enucleating an oocyte of a first mammalian species and transferring the nucleus of the primary cell into said oocyte; b) activating the NT unit; c) culturing the activated NT unit in a immunocomprimized mouse to produce a teratoma; and d) isolating a differentiated cell from said teratoma, does not reasonably provide enablement for use of any source of host cell from a first species, nor the use of any organism besides a mammalian species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The basis of the rejection is not directed towards the intended use of said cells, rather to the nature and breadth of claimed invention. The recitation of cells 'that can be subsequently implanted for therapy' is not being interpreted as an intended use but rather as a characteristic of the cells. The claims are drawn to a method of nuclear transfer wherein the resulting differentiated cell represents a rejuvenated primary cell. The claims are broad drawn to any organism, including animals and plants. The specification teaches the production of cells by use of nuclear transfer into an oocyte, and relies in great part on specific teachings in the prior art to practice the claimed process. The specification provides examples for the production of a cell using nuclear transfer methodology of a first mammal transfer transferred into an oocyte. The specification teaches that the resulting cell has increased telomere and telomerase activity. In

view of the art of record, it is noted that only the use of oocytes has been fully enabled for use as a enucleated donor. In addition, the claims embrace use of any organism as either nuclear donor and cell source recipient (plant, human, yeast, ...).

The nature of the invention requires that the donor nucleus be 'reprogrammed' such that totipotency or pluripotency is achieved. At the time of filing the art required that the donor nucleus be in contact with the cytoplasm of an oocyte. Kono teaches that a break down of the nuclear envelop is necessary for reprogramming, as reprogramming probably requires the contact of chromatin with the ooplasm (page 76, second column, lines 1-6). Wolf *et al.* states, as in support of Kono, that a donor nucleus is reprogrammed by the recipient cytoplasm where the donor nucleus is reverted to the same morphological and temporal pattern of the zygote (page 102 first column, lines 1-4). Further, it is recognized that the oocyte would need to be enucleated so that the developing embryo would retain the correct ploidy. To this end, Wolf *et al.* teach that the coordination between cell cycles of donor and recipient cell is important to avoid DNA damage and maintain correct ploidy of the resulting embryo (page 10, second column, lines 1-5).

Examiner would agree that the examples recited in the instant specification are enabled by the methodology commonly practiced in the art, however the claims are not limited to these enabled embodiments. The only enabled donor cell in the art is a mammalian oocyte, and the instant specification fails to provide a nexus for use of any other type of donor cell or in any other organism beside a mammal. A review of the art by the Examiner does not indicate that nuclear transfer has been successfully performed in any other organism besides a mammal. In light of

Applicant's reliance on the art for practice of the claimed process and resulting cell, the instant specification and the art of record fails to provide the necessary guidance which would enable the artisan to practice the invention commensurate in scope as instantly claimed.

Additionally, claims 25-39 are drawn to propagating the cell in a target species and into an animal. In light of the teaching of the instant specification, the implantation and propagation is intended to be into a pseudopregnant female host wherein the host is the same as the donor nuclei, however, the claims embody transfer into any organism. With regard to the specific teachings in the specification, the art would fully enable the transfer of a NT unit comprising a enucleated oocyte from a first mammal and the nucleus/mitochondria from a second mammal into a pseudopregnant female of the same species of the second mammal. However, there is no teaching in the specification nor the art of record which demonstrates the necessary guidance needed to transplant a developing embryo into a species with a different genetic background (i.e mouse nuclei/mitochondria into a host cow). Further, the full breadth of the claims encompass the transplantation into any area of the targeted species, in any species. It is well recognized in the art that transplantation of cells across various species, i.e. xenotransplantation, has not been successfully performed except into immunocomprimized animals, then usually to a immunoprivaledged region of said animal. In view of the lack of guidance in the instant specification to perform these processes, and in light of the art recognized limitations of xenotransplantation, it would require undue experimentation for the artisan to practice the full scope of the invention as claimed.

In the detailed description of the invention, it is stated that the invention provides a method for rejuvenating primary cells through nuclear transfer techniques (page 1; first lines). The invention, in great part, relies on Applicants observation that practicing nuclear transfer methods, that a donor cell nucleus can be reprogrammed to become a pluripotent cell when transferred into an oocyte and properly cultured. However, the specification fails to teach how the art taught and practiced methods of nuclear transfer differ from those instantly claimed. The specification clearly indicate the reliance of the art to practice the instant invention, and thus, the only working embodiments which are enabled are those specifically supported by the art. Lacking the necessary guidance, the specification fails to provide a nexus between art recognized limitations and the ability to practice the full scope of the invention as presently claimed.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and the state of the art at the time of the claimed invention was made, it would have required one of skill in the art undue experimentation to practice the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claim 1 is unclear in the recitation of a 'rejuvenating a primary cell' because the method as claimed does not result in modifying the cell *per se*, rather results in a different and unique cell. The method as instantly claimed encompasses nuclear transfer techniques wherein the nucleus of the first cell is transferred into a second recipient cell. Once the genetic material is removed from the first cell it is no longer a cell, nor when it is transferred to the recipient cell is it the same cell, rather it is a chimeric cell. Further, in the formation of a teratoma, it is recognized in the art that the cells often do not maintain the proper ploidy or the properties of terminally differentiated cell. While it is not contested that following the instantly claimed method steps the artisan could obtain a cell which resembles cell type of the initial primary cell, however it is unclear if this represents a rejuvenated form of the initial cell. Further, a common property of many primary cells is terminal differentiation wherein the cell no longer proliferates. For example, in view of claim 2, it is unclear if the rejuvenated primary cell would also be terminally differentiated, and if unable to proliferate would it still be considered rejuvenated? Though the method steps are straightforward and clear, the metes and bounds of what a rejuvenated primary cell is, and if practicing the steps results in said cell is unclear.

Claim 3 is confusing because the antecedent basis of the second control teratoma is unclear. It is unclear if the teratoma is generated by the primary cell, the recipient oocyte or the ICM.

Claim 4 is unclear because it depends on itself. For the sake of compact prosecution it will be interpreted as being dependent on claim 3.

Claim 7 is vague and unclear because the nature of the alteration of the genome is not adequately described. It is unclear if a modification is made to the primary cell, the rejuvenated primary cell and when the modification is introduced. Dependent claims 17-20 are included in this rejection because they fail to clarify the basis of the rejection.

Claim 8 is confusing because the antecedent basis of the second control teratoma in the final step is unclear. It is unclear if the teratoma is generated by the primary cell, the recipient oocyte or the ICM..

Claim 13 is unclear in the recitation of '(for transplantation into a patient in need of a transplant)' because it is unclear if this is an intended use for the tissue or a limitation wherein the tissue generated must be capable of being transplanted.

Claim 25 is confusing and unclear because an animal with the same genotype can not be genetically different so can not be altered. From the recited method steps it is unclear how the animal genetically altered.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-39 are rejected under 35 U.S.C. 102(a/e) as being anticipated by Strelchenko *et al.* (US Patent 6,011,197) or Damiani et al. (US Patent 6,258,988) as further evidenced by Evans *et al.* (Nature Genetics 23:90-93).

Presently, claims 1-39 encompass a method for rejuvnentating a cell by the use of nuclear transfer technology. The method as instantly claimed is subject to 35 USC 112, first and second paragraph, rejections, in light of the teachings of the instant specification and the specific steps recited in instant claims, the method is drawn generally to the use of nuclear transfer methods to generate a primary cell. In view of 35 USC 112, second paragraph, issues the breadth of the claim can reasonably interpreted to encompass a method of nuclear transfer and isolation of a differentiated cell from a teratoma. In addition, dependent claims are drawn to genetically modifying the rejuvenated cell. Again, in view of 35 USC 112, second paragraph, issues the breadth of the claim can reasonably interpreted to encompass any form of genetic modification.

Strelchenko *et al.* teach a method of nuclear transfer wherein the resulting cell is used in methods to clone a bovine. Dimiani *et al.* teach a method of nuclear transfer wherein the resulting cell is used in methods to clone an ovine. Further, Strelchenko *et al.* and Dimiani *et al.* teach that the methodology can be used to generate an animal in which a heterologous sequence is introduced. In addition, though Strelchenko *et al.* and Dimiani *et al.* do not specifically teach that

they transfer or exchange of heterologous genetic material from the mitochondria, at the time of the claimed invention it was recognized that in performing nuclear transfer techniques that enucleation and the transfer of nuclei resulted in the exchange of mitochondria as evidenced by Evans *et al.* The specification relies on the methods taught in the art for the practice of the claimed invention, and since practicing the methods inherently transferred mitochondria, the methods of Strelchenko *et al.* and Dimiani *et al.* anticipate the claims. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). In the instant case, it is unclear how the instantly claimed methods and the resulting cells from said methods are materially different from the methods of nuclear transfer known and taught in the art. Thus, the methods taught in Strelchenko *et al.* and Dimiani *et al.* anticipate the instantly claimed methods and cells produced by said method.

Claims 1-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Robl *et al.* (WO 98/07841) as evidenced by Evans *et al.* (Nature Genetics 23:90-93).

Claims 1-39 are summarized above. Robl *et al.* teach a method of cross-species nuclear transfer wherein the resulting cell is chimeric cell comprising an enucleated oocyte which is different from that of the transferred nuclei. Robl *et al.* do not specifically teach that they transfer any specific amount of mitochondria, however at the time of the claimed invention it was recognized that in performing nuclear transfer techniques that enucleation and the transfer of nuclei resulted in the exchange of mitochondria as evidenced by Evans *et al.* The specification relies on the methods taught in the art for the practice of the claimed invention, and since practicing the methods inherently transferred mitochondria, the methods of Robl *et al.* anticipate the claims as they are drawn to generating a genetically modified cell. As noted above, where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product (*In re Ludtke*). Whether the rejection is based on "inherency" under 35 USC 102, on "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972). In the instant case, it is unclear how the instantly claimed methods and the resulting cells from said methods are

materially different from the methods of nuclear transfer known and taught in the art. Thus, the methods taught in Robl *et al.* anticipate the instantly claimed methods and cells produced by said method.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach, whose telephone number is (703) 305-3732. The examiner can normally be reached on Monday through Friday from 8:00 to 4:30 (Eastern time).

If attempts to reach the examine by telephone are unsuccessful, the examiner's supervisor, Karen M. Hauda, can be reached on (703) 305-6608. The fax number for group 1600 is (703)308-4724.

An inquiry of a general nature or relating to the status of the application should be directed to Kay Pinkney whose telephone number is (703) 305-3553.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice

published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Deborah Crouch

Joseph T. Woitach

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